REMARKS

Applicants respectfully request entry of the amendments and remarks presented herein. Claims 1, 2, 7, 9, 11, 13, 14 and 19 stand rejected. Claims 2, 14, and 19 are cancelled herein without prejudice. Claim 1 is amended to recite an isolated nucleic acid molecule consisting essentially of a variant *ASMT* nucleic acid sequence, wherein the variant *ASMT* nucleic acid sequence is: (a) at least fifteen contiguous nucleotides of SEQ ID NO:1, wherein the sequence includes one or more of nucleotide positions 8011, 12327, and 23936 of SEQ ID NO:1, with the proviso that the nucleotide at position 8011 of SEQ ID NO:1 is thymine, the nucleotide at position 12327 of SEQ ID NO:1 is cytosine, or the nucleotide at position 23936 of SEQ ID NO:1 is thymine; or (b) the complement of (a). Support for this amendment can be found, for example, in original claims 7, 9, and 11, which are amended herein for consistency with amended claim 1. Support also can be found in Applicants' specification at page 7, lines 18-24, which disclose that a nucleic acid can have a length from about 8 nucleotides to greater than 1000 nucleotides (*e.g.*, 15 nucleotides), and that a nucleic acid can be complementary to an *ASMT* reference sequence. In addition, claim 13 is amended herein to incorporate the language of original claim 14.

New claims 20-23 are added herein. Claims 20 and 21 recite that the isolated nucleic acid molecule of claim 1 is from 15 to 100 or from 20 to 50 nucleotides in length, respectively. Claim 22 recites a vector comprising the isolated nucleic acid of claim 1, and claim 23 recites that the isolated nucleic acid molecule comprised by the vector is from 20 to 50 nucleotides in length. Support for claims 20-23 can be found in Applicants' specification at, for example, page 7, lines 18-21, which disclose that a nucleic acid can have a length from about 8 nucleotides to greater than 1000 nucleotides, and at page at page 13, lines 22-30 and page 15, lines 3-28 discloses that nucleic acids can be incorporated into vectors. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 7, 9, 11, 13, and 20-23.

Objection to the Specification

The Examiner objected to the specification for containing an allegedly vague description of the term "arsenic methyltransferase (*ASMT*) nucleic acid sequence." The Examiner stated that the specification at page 6, line 24 describes the *ASMT* nucleic acid sequence as including a nucleotide sequence variant and nucleotides flanking the sequence variant. The Examiner asserted that this genus comprises a subgenus of nucleotide sequence variants and variants of nucleotides flanking the genomic DNA of SEQ ID NO:1, wherein the variant sequences have substitutions of nucleotides 8011, 12327, and 23936 of SEQ ID NO:1, and also substitutions of nucleotides in the regions flanking these nucleotides. The Examiner further asserted that one of skill in the art would be confused as to how a sequence that is to be changed at positions 8011, 12327, or 23936 can be only 10 nucleotides in length, and how a sequence that is only 10 nucleotides in length can encode an enzyme having ASMT activity.

Applicants respectfully disagree. The description of an *ASMT* nucleic acid sequence is clear. Given the remarks below with regard to the rejections under 35 U.S.C. § 112, second paragraph, Applicants submit that the Examiner's comments have been addressed.

Rejections under 35 U.S.C. §112

The Examiner rejected claims 1, 2, 7, 9, 11, 13-14 and 19 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner asserted that the phrase "comprises a nucleotide sequence variant in position X of SEQ ID NO" is confusing, and that Applicants do not disclose sequence that comprise in the recited positions an insertion of any variant nucleotide sequence. The Examiner further asserted that the claims are confusing in reciting "said nucleic acid molecule is at least ten nucleotides in length," and "comprises a nucleotide sequence variant at a position selected form the group consisting of position 8011, 12327 and 23936 of SEQ ID NO:1." The Examiner alleged that a person of skill in the art would be confused as to how a sequence that is to be changed at position 8011, 12327, or 23936 can be only 10 nucleotides in length. In addition, the Examiner alleged that it is confusing how a sequence that is only 10 nucleotides long can encode an enzyme having ASMT activity.

Applicants respectfully disagree. First, Applicants note that neither the previous claims nor the present claims require the recited nucleic acid molecules to have ASMT activity.

Second, neither the previous claims nor the present claims require the nucleic acid molecules to include substitutions at all three of the recited positions. Rather, previous claim 1 recited a Markush group of nucleotide sequence variants, while present claim 1 recites, *inter alia*, that the sequence includes one or more of nucleotide positions 8011, 12327, and 23936 of SEQ ID NO:1, with the proviso that the nucleotide at position 8011 of SEQ ID NO:1 is thymine, the nucleotide at position 12327 of SEQ ID NO:1 is cytosine, or the nucleotide at position 23936 of SEQ ID NO:1 is thymine. A person of skill in the art would understand that the recited nucleic acid molecules include at least fifteen nucleotides in proximity to at least one of the recited positions, with a substitution at at least one of the recited positions, but not necessarily at each of the recited positions. A person of skill in the art also would understand that positions are given with respect to SEQ ID NO:1, and as such, a nucleic acid molecule can contain position 8011 of SEQ ID NO:1 without being over 8000 nucleotides in length. Thus, the claims are clear and definite.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 7, 9, 11, and 13 under 35 U.S.C. §112, second paragraph.

The Examiner rejected claims 1, 2, 7, 9, 11 and 19 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleged that the claims are directed to a large genus of DNA molecules for which the function and structure are not sufficiently described. The Examiner further alleged that inclusion of the phrase "variant in positions 8011, 12327, and 23936" without an identifying fragment of SEQ ID NO:1 "is referring to any nucleotide sequence one can think of."

Applicants respectfully disagree. The specification adequately describes the nucleic acid molecules recited in the previous claims. Contrary to the Examiner's assertion, the recitation of "a nucleotide sequence variant at a position selected from the group consisting of position . . . 8011, . . . 12327, . . . [and] 23936 . . . of SEQ ID NO:1" in previous claim 1 does not refer "to any nucleotide sequence one can think of." Rather, previous claim 1 referred to a nucleic acid sequence having a variant at any of the recited positions within SEQ ID NO:1, selected from a group including positions 8011, 12327, and 23936 of SEQ ID NO:1. To further prosecution, however, claim 1 has been amended to recite an isolated nucleic acid molecule consisting essentially of a variant *ASMT* nucleic acid sequence, wherein the variant *ASMT* nucleic acid

sequence is (a) at least fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes one or more of nucleotide positions 8011, 12327, and 23936 of SEQ ID NO:1, with the proviso that the nucleotide at position 8011 of SEQ ID NO:1 is thymine, the nucleotide at position 12327 of SEQ ID NO:1 is cytosine, or the nucleotide at position 23936 of SEQ ID NO:1 is thymine; or (b) the complement of (a). Thus, claim 1 as amended requires the nucleic acid molecule to contain at least fifteen contiguous nucleotides that are identical to a portion of SEQ ID NO:1 in the area of the recited nucleotides, with the exception that the sequence contains the recited variant nucleotide.

Applicants note that nucleic acid molecules "consisting essentially of" the recited variant sequences have the basic and novel characteristic that they are able to distinguish, based upon hybridization, a nucleic acid having a sequence that contains the recited variant from a nucleic acid having a sequence that does not contain the variant (e.g., the wild type sequence). Applicants further note that the claimed nucleic acid molecules can include additional sequences or labels (e.g., a fluorescent label as disclosed at page 23, lines 6-7 of Applicants' specification), provided that such additions do no affect the basic and novel characteristic of the nucleic acid molecules.

For claims drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species. Description of a representative number of species does not require the specification to provide individual support for each and every species that the genus embraces. *See, e.g., In re Angstadt*, 537 F.2d 498, 502 (Cust. & Pat. App. 1976), and MPEP § 2163. Applicants' specification provides sufficient written description for the presently claimed nucleic acid molecules. For example, Applicants' specification discloses the nucleotide sequence of SEQ ID NO:1. Thus, it is clear that Applicants were in possession of numerous fifteen nucleotide sequences that include positions 8011, 12327, and 23936 of that sequence. As such, Applicants' specification provides a representative number of nucleic acid molecules consisting essentially of the recited variant sequences. Further, Applicants' specification discloses that a nucleic acid molecule can include an additional sequences or labels (*e.g.*, a fluorescent label, a tag sequence at one or both ends, or a non-SEQ ID NO:1 sequence such as a restriction site) that permit the nucleic acid molecule to function in a differential hybridization setting. *See, e.g.*, Applicants' specification at page 15, lines 9-17, page

22, lines 7-24, and page 28, lines 11-15. Thus, a person of ordinary skill in the art would have appreciated that Applicants invented and were in possession of the nucleic acid molecules recited in the present claims.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1, 7, 9, and 11 under 35 U.S.C. §112, first paragraph.

The Examiner rejected claims 1, 2, 7, 9, 11 and 19 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. The Examiner stated that the specification is enabling for nucleic acid molecules that are allelic variants of SEQ ID NO:1 having nucleotides in positions 8011, 12327, and 23936 changed, but is not enabling for any nucleic acid molecule that is at least ten nucleotides in length and comprises nucleotide sequence variants at positions 8011, 12327, and 23936 of SEQ ID NO:1.

Applicants respectfully disagree. The previous claims were fully enabled. Nevertheless, claim 1 is amended herein to recite an isolated nucleic acid molecule consisting essentially of a variant ASMT nucleic acid sequence, wherein the variant ASMT nucleic acid sequence is (a) at least fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes one or more of nucleotide positions 8011, 12327, and 23936 of SEQ ID NO:1, with the proviso that the nucleotide at position 8011 of SEQ ID NO:1 is thymine, the nucleotide at position 12327 of SEQ ID NO:1 is cytosine, or the nucleotide at position 23936 of SEQ ID NO:1 is thymine; or (b) the complement of (a).

Applicants' specification fully enables claim 1. The utility of the claimed nucleic acid molecules is clear, particularly with regard to the recited polymorphisms. The fact that additional sequences (e.g., tag or primer sequences) can be added to one or both ends does not change the basic utility of the nucleic acid molecules and the polymorphisms contained therein. In fact, a person of ordinary skill in the art reading Applicants' specification would readily have been able to ascertain whether and what nucleotides could be added to one or both ends of a variant-containing nucleotide sequence from SEQ ID NO:1 in order to use the nucleic acid molecule for a particular procedure. For example, a person of ordinary skill could add a tag sequence to one or both ends of a nucleic acid molecule for manipulation (e.g., purification) of the nucleic acid. See, e.g., Applicants' specification at page 15, lines 9-17 and page 28, lines 11-

15. Further, a person of ordinary skill could design a primer containing at least a fifteen nucleotide sequence of SEQ ID NO:1 with or without a variant nucleotide at its 3' end, and a non-SEQ ID NO:1 sequence (e.g., a restriction site) at its 5' end, and could use the primer for allele specific PCR, for example. See, e.g., Applicants' specification at page 23, lines 10-25. In addition, a person of ordinary skill could design a primer containing at least a fifteen nucleotide sequence of SEQ ID NO:1 with or without a variant nucleotide, and a fluorescent label, and could use the probe for allele specific hybridization. See, e.g., Applicants' specification at page 22, lines 7-24. Thus, no undue experimentation would have been required for a person having ordinary skill in the art to use the presently claimed nucleic acids.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1, 7, 9, and 11 under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §102

The Examiner rejected claim 13 under 35 U.S.C. §102(b) as allegedly being anticipated by the Lin *et al.* reference (*J. Biol. Chem.* (2002) 277:10793-10803) and the Strausberg *et al.* reference (*Proc. Natl. Acad. Sci. USA* (2002) 99:16899-16903). The Examiner asserted that the cited references disclose ASMT enzymes from rat and mouse, and that the amino acid sequences of these ASMT enzymes anticipate the genus recited in claim 13.

To further prosecution, Applicants have amended claim 13 to incorporate the language of previous claim 14. Thus, claim 13 recites that the amino acid sequence variant is a tryptophan at residue 173, a threonine at residue 287, or an isoleucine at residue 306. At no point does the Lin *et al.* reference or the Strausberg *et al.* reference disclose a nucleic acid sequence encoding a polypeptide that contains an amino acid sequence variant as recited in present claim 13. Thus, claim 13 is novel over the cited references.

In light of the above, Applicants respectfully request withdrawal of the rejection of claim 13 under 35 U.S.C. § 102(b).

Information Disclosure Statement

Applicants note that a Supplemental Information Disclosure Statement was filed on January 30, 2006. A copy of the Form PTO-1449 is attached hereto for the Examiner's

convenience. Applicants respectfully request the Examiner to review the reference listed on the Form PTO-1449 and return an initialed copy of the form to the undersigned agent.

CONCLUSION

Applicants submit that claims 1, 7, 9, 11, 13, and 20-24 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: February 1, 2007

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